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***IN VITRO* RELEASE OF DICLOFENAC SODIUM FROM  
DIFFERENT TOPICAL VEHICLES**

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**ABSTRACT**

There is currently a great deal of world-wide interest in the field of transdermal drug delivery and, consequently, broad classes of drugs are being evaluated for percutaneous absorption potential. The advantages of this mode of drug administration are numerous, the patient convenience and therapeutic optimization of using patch transdermal systems being major positive features. The *in vitro* release test is a measure of in process control and also as a finished product specification for example, ointment, cream and gels. An *in vitro* diffusion cell experiment was designed to demonstrate the rate of release of Diclofenac sodium from three different topical vehicles: (i) an oil in water cream (ii) a gel; and (iii) an ointment. *In vitro* release of Diclofenac sodium from three different bases to an aqueous receptor phase through cellophane membrane was monitored spectrophotometrically. By monitoring and attempting to explain the numerous possible from the three vehicles, it was a better to understanding of the complexities of transdermal drug administration. More over gel topical vehicles could be suggested as a good candidate for the topical delivery of Diclofenac sodium, giving higher drug release than the cream and ointment formulations.

**Key words:** Diclofenac sodium, Vehicles, *In vitro* diffusion, Transdermal.

**INTRODUCTION**

When taken orally, many drugs are destroyed by the liver. Drug administration through the skin often provides a slower, more controlled alternative route for release into the blood stream. There is currently a great deal of world-wide interest in the field of transdermal drug delivery and, consequently, broad classes of drugs are being evaluated for percutaneous absorption potential. The skin is the largest human organ. It ensures that harmful substances and drugs released from topically applied formulations cannot intrude into the organism offhand.<sup>[1]</sup> The evolutionary development of the human skin as a

potential protective barrier keeping water in and noxious substances out of the human body was a requirement for terrestrial life.<sup>[2]</sup> Drug delivery through the skin has been used to target the epidermis, dermis and deeper tissues and for systemic delivery. The major barrier for the transport of drugs through the skin is the stratum corneum, with most transport occurring through the intercellular region. Another potential advantage of this type of drug delivery is the optimization of drug concentration at the desirable sites, reducing the chances of side effects.<sup>[3]</sup> Therapeutic efficacy of any topical formulation depends on its ability to deliver drugs to their sites of action from the skin surface for either local or systemic purposes.<sup>[4-5]</sup> The efficacy of topically applied drugs is often limited by poor skin penetration<sup>[6]</sup>. Several factors are known to influence the rate and extent of drug absorption through skin like mode of application, skin condition, vehicle used, concentration and physicochemical properties of drug molecules.<sup>[7]</sup> It is generally assumed that the nature of the vehicle strongly influences the rate and extent of drug release. Release may be improved by selecting the appropriate vehicle. The best vehicle for topical use has been described as the one which contributes a reversible decrease in the stratum corneum resistance and allows the diffusion of molecules into the vehicle itself.<sup>[8]</sup> Diclofenac sodium (2-[2-[(2, 6-dichlorophenyl) amino] phenyl] acetic acid) is a potent member of non-steroidal anti-inflammatory drugs (NSAIDs) and widely used clinically, because of its strong analgesic and anti-pyretic effect.<sup>[9]</sup> It has a short half-life (2 hrs). Diclofenac sodium causes gastrointestinal disturbances, peptic ulceration with bleeding, if present in large doses in gastrointestinal tract (GIT).<sup>[10]</sup> It is marketed as injections, oral sustained release tablets and topical formulations. After oral administration, it is extensively metabolized in the liver and because of its short biological half-life, the drug has to be administered frequently.<sup>[11]</sup> The topical application allows for a higher local concentration of the drug at the site of initiation of the pain and lower or negligible systemic drug levels producing fewer or not adverse drug effects.<sup>[12]</sup> As it is not easily absorbed on dermal application many strategies have been suggested in order to overcome the low permeability of drug through the skin.<sup>[13-15]</sup> In developing drug preparations for topical delivery through the skin, the choice of vehicle formulations for a given drug can greatly influence the rate and extent of drug permeation across the skin.<sup>[16-17]</sup> Topical drugs

used to control pain act locally on damaged or dysfunctional soft tissues or peripheral nerves, and their actions may be on the inflammatory response itself or on sensory neurons.<sup>[18]</sup> An improved Diclofenac formulation with a high degree of skin permeation could be useful in the treatment of not only locally inflamed skin tissues, but also inflammatory and painful states of supporting structures of the body bones, ligaments, joints, tendons and muscles.<sup>[19-20]</sup>

### Objective & Hypothesis

Stratum corneum is the principal barrier for cutaneous penetration allowing slow absorption for the majority of drugs. The objective of the present investigation was to deliver the Diclofenac sodium topically as a cream, gel and ointment. So hypothesis for the present work is that the drug may be penetrating more by the use of different vehicles on topical application.

### MATERIALS AND METHODS

Diclofenac sodium was obtained as the gift sample from Alembic Pharmaceutical limited, Baroda, Gujarat, India. All other chemicals were used of analytical grade.

#### Formulation of cream, gel and ointment<sup>[21]</sup>

The Diclofenac sodium was incorporated into the three different vehicles (ointment F1, cream F2 and gel F3) at a concentration of 1 percent by geometric trituration. The three bases were chosen for their different hydrophilic, hydrophobic and viscosity characteristics.

**Table 1: Formulation for Ointment (F1)**

Ingredients	Quantity
Diclofenac sodium	1%
Emulsifying wax	6g
White soft paraffin	10g
Liquid paraffin	4g
Sodium hydroxide	0.02g
Methyl p-Hydroxy benzoate	0.04g

**Procedure:** Melt emulsifying wax in a porcelain dish, on a water bath. To this melt, incorporate liquid paraffin, white soft paraffin and add other ingredient & drug (1%) one

by one with continuous stirring. Remove the foreign particle if present by decanting or straining to a hot vessel and stir until product becomes cool and a semisolid mass is obtained.

**Table 2: Formulation for Cream (F2)**

Ingredients	Quantity
Diclofenac sodium	1%
Stearic acid	15g
Potassium hydroxide	0.50g
Sodium hydroxide	0.18g
Cetyl alcohol	0.5g
Propylene glycol	3g
Glycerin	1ml
Methyl p-Hydroxy benzoate	0.04g
Water	14.88ml

**Procedure:** Take ingredients of oil phase and heat at 70°C in container. Take ingredients of aqueous phase add heat also at 70°C in container. Now add aqueous phase in to organic phase with constant stirring, cool the solution. Add perfuming agent when temperature is 35°C.

**Table 3: Formulation for Gel (F3)**

Ingredients	Quantity
Diclofenac sodium	1 %
Carbopol 940	0.2g
Triethanol amine	0.1g
Methyl p-Hydroxy benzoate	0.04g
Glycerin	2ml
Purified water	17.4ml

**Procedure:** Specific amount of Carbopol 940 was soaked in water overnight. The required amount of drug (1%) was dissolved in this solution with stirring at 500 rpm by magnetic stirrer for 1 hour. Carbopol was then neutralized with 0.5% triethanolamine.

Methyl p-Hydroxy benzoate was added as preservative. Glycerin 10% was added slowly with stirring to obtain a clear gel.

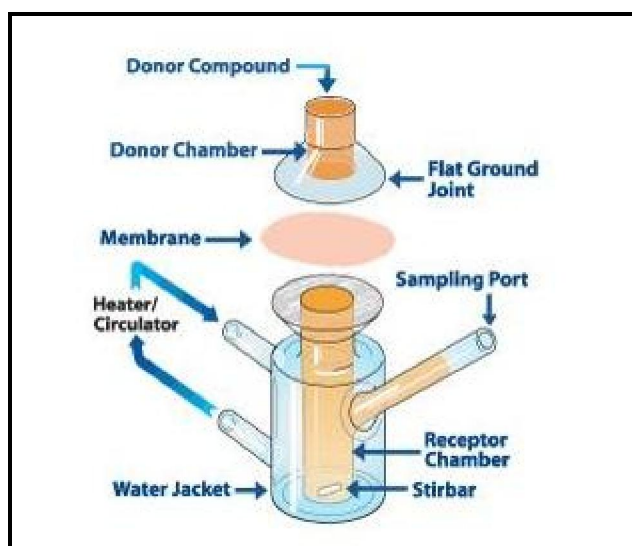
## EVALUATION PARAMETERS <sup>[22-24]</sup>

### Stability study

All three products were placed for stability study for three months at room temperature and at refrigerator temperature for the evaluation of physical characteristics of products like colour change, phase separation, consistency & development of disagreeable odour.

### *In-vitro* release studies

Franz Cells, Horizontal Cells like the Crown Glass Side-Bi-Side cells, and related equipments are used for studying membrane transport and drug diffusion through biological and synthetic membranes. Applications include experimentation in the areas of drug discovery, drug transport, drug screening, controlled release, formulation optimization, dermatology, skin toxicology, oral absorption, buccal absorption, percutaneous absorption, equilibrium dialysis and protein binding.



**Figure 1**  
A Franz diffusion cell

Approximately 1 g of medicated formulation was packed into each of three cell donor chambers for all three formulations, ensuring that there were no air bubbles between the formulation and donor surface of the cellophane membrane. The receptor phase was filled with phosphate buffer pH 6.8 and continuously stirred with a small

magnetic bead at a speed of 100 rpm during the experiments to ensure homogeneity and temperature was maintained at  $37 \pm 0.5$  °C. The samples were withdrawn at various time intervals and analyzed spectrophotometrically at 276 nm. Release pattern of all three different formulations are shown in figure 2.

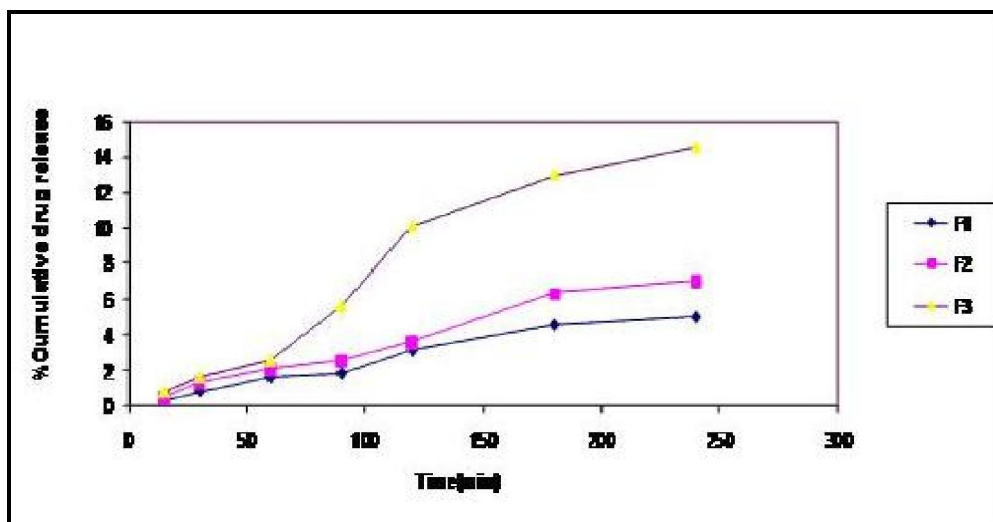
## RESULTS AND DISCUSSION

### Stability study

There was no evidence of phase separation, development of disagreeable odour, change in colour and consistency of the all three products during stability study for three months at both room temperature and at refrigerator temperature.

### *In-vitro* release studies

Different release profile of Diclofenac sodium was observed due to the different vehicles examined. According to the release study, the highest drug release obtained with gel formulation. The gel formulation appears to present the ideal combination of solubility and physical diffusivity through the vehicle, yielding the highest drug release rate.



**Figure 2**  
Effect of vehicles on *In vitro* release  
F1 = Ointment, F2 = Cream, F3 = Gel

## CONCLUSION

In the present study, topical delivery of the Diclofenac sodium in a cream, gel and ointment base were studied. From the above work, gel topical vehicles could be

suggested as a good candidate for the topical delivery of Diclofenac sodium, giving higher drug release compared to the cream and ointment formulations.

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